

JUL 07 2008

Application Number 10/538858

Response to the Office Action dated April 4, 2008

REMARKS

Favorable reconsideration of this application is requested in view of the following remarks.

Claims 1 and 5 have been amended to remove the indefinite language as supported by original claims 1 and 5 and the specification at pages 26-28, the first paragraphs of Examples 4, 5, and 6 and page 4, lines 27-28; and claims 1, 4 and 6-29 have been amended editorially.

Claims 2 and 3 have been canceled and corresponding claims 30 and 31, respectively, that include editorial revisions have been added.

Claims 1-5 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection.

Claims 1 and 5 have been amended to remove the language "substantially free of impurities." In addition, claims 1-4 have been amended to include a period at the end of each claim. Therefore, this rejection should be withdrawn.

Claims 1-29 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Monsalvatje Llagostera, et al. (EP Patent Application Publication No. EP 0,992,495) in view of U.S. Department of Health and Human Services (Guidance for Industry: Q3C – Tables and List). Applicants respectfully traverse this rejection.

EP '495 discloses a toluene solvate of quinapril HCl and an ethyl formate solvate or a methyl acetate solvate thereof (see paras. 0020 and 0022). In the reference, quinapril HCl benzyl ester is dissolved in isopropanol, then this solvent is removed, and toluene is added in order to obtain precipitation of a toluene solvate (see paras. 0017-0018). However, this toluene solvate includes an impurity diketopiperazine and needs a purification process to remove that impurity (see paras. 0015-0018). Because toluene is a class 2 solvent, which is more toxic than a class 3 solvent, the class 3 solvent such as

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ethyl formate or a methyl acetate is used to purify the crude toluene solvate (see paras. 0020-0021). However, flash points of ethyl formate and methyl acetate are -20 °C and -16 °C, respectively (see page 4, lines 16-22 and page 18, lines 6-10 of the specification), and due to such too low flashing points, these solvents cannot be used for a commercial scale production (*Id.*). In contrast, claim 1 requires a nitroalkane solvate of quinapril HCl, which is a pure product crystallized and purified with a nitroalkane solvent after hydrogenolysis (i.e., converting to quinapril HCl) (see claim 5 and page 4, lines 27-28 and page 18, lines 1-5 and 11-18 of the specification). Therefore, the nitroalkane solvent is not interchangeable with either of toluene, ethyl formate or methyl acetate, i.e., a nitroalkane solvate of quinapril HCl is not interchangeable with a toluene solvate, an ethyl formate solvate, or a methyl acetate solvate thereof, because toluene is used for precipitation of quinapril HCl and ethyl formate and methyl acetate are used only for purification thereof but nitroalkane can be used for crystallization and purification of quinapril HCl. Accordingly, claim 1 is distinguished from EP '495.

With respect to a production method, EP '495 discloses a two-solvent process that needs two types of solvents for precipitation and purification after hydrogenolysis such as toluene and a class 2 solvent as discussed above. In contrast, in claim 5, quinapril benzyl ester is dissolved in an alcoholic solvent with HCl or a hydrochloric acid for hydrogenolysis, and then, crystallized and purified with a nitroalkane solvent. Pure nitroalkane solvate of quinapril HCl is obtained with the nitroalkane. Therefore, the method in claim 5 is distinguished from EP '495.

Guidance for Industry: Q3C – Tables and List was published in November 2003, i.e., after December 16, 2002, the PCT filing date of the present application. Accordingly, Guidance for Industry is not available as prior art against the present application.

Accordingly, this rejection of claims 1-29 should be withdrawn.

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In view of the above, Applicants request reconsideration of the application in the form of a Notice of Allowance.



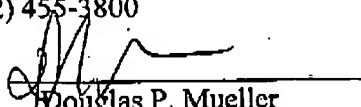
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